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Squamous Cell Carcinoma Sinonasal: A Case Report

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Abstract: ***Introduction: Squamous cell carcinoma (SCC) of the nasal and paranasal sinuses (SNSCC) is the most common histologic subtype of all sinonasal tumors. It arises from mucosal sites throughout the paranasal sinuses, namely nasal cavity to maxillary sinus. Preoperative histologic diagnosis of a given sinonasal lesion is essential to correctly plan a proper treatment strategy. Multimodality therapy regimens, including surgery, radiotherapy (RT), and/or chemotherapy, are frequently utilized in the treatment of these tumors. Case report: A 43rd years old male, came to the ENT outpatient department with a chief complain of a mass on the nose since one and a half years before. He was diagnosed with SCC sinonasal stage IVA, after a tumor biopsy. He was scheduled for chemotherapy at April 8th 2024 with Paclitaxel 270 mg and Carboplatin 690 mg and scheduled for the second chemotherapy at April 30th 2024. Discussion: SNSCC is a complex disease, and its pathogenesis is poorly understood. Histologic diagnosis of SNSCCs can be challenging due to relative rarity, a large miscellany of different possible histology, and overlapping appearance of other malignancy or inflammatory disease. Surgery is a potentially curative treatment for resectable SNSCC. To achieve negative surgical margins, the use of induction chemotherapy has been investigated as part of multimodal treatment.***

Keywords: sinonasal, squamous cell carcinoma, SCC, SCC sinonasal

1. Introduction

*Squamous cell carcinoma (*SCC) of the nasal and paranasal sinuses (SNSCC) is the most common histologic subtype of all sinonasal tumors, making up more than 50% of cases. SNSCC arise from mucosal sites throughout the paranasal sinuses, namely nasal cavity to maxillary sinus. While the incidence of SNSCC is decreasing, 5 - year overall survival (OS) rates have not changed appreciably over the last three decades, hovering around 50%. This is in part due to the advanced stage of disease at diagnosis and high rate of local recurrence. When outcomes are sub - stratified by tumor site, patients with nasal cavity SCC have improved 5 - year relative survival (RS) (74.5%) compared with patients with maxillary sinus SCC (35%) and ethmoid sinus SCC (33%). Frontal and sphenoid sinus SCC carry the worst prognosis with 5 - years survival of 30%. Across all tumors, increased age, T and N classification is associated with worse overall survival (OS). The incidence of SNSCC arising as a second primary in head and neck cancer patients is low (0.2%). [1, 2]

A recent study on 4994 SNSCC registered at the United States National Cancer Institute's Surveillance, Epidemiology, and End Results revealed an incidence of 0.32 new cases/100, 000 habitants/year, with a steadily declining trend of −2.6%/year over the last 3 decades. In patients with neither regional nor distant metastasis, 5 - , 10 - , 15 - , and 20 - year overall survival (OS) rates were 82.9%, 73.8%, 60.6%, and 43.7%, respectively. SNSCC with nodal metastases and those with distant disease showed 5 - , 10 - , 15 - , and 20 - year OS rates of 41.1%, 32.8%, 26.2%, and 22.5%, and 29.2%, 19.8%, 18.3%, and 17.1%, respectively. [3]

Preoperative histologic diagnosis of a given sinonasal lesion is essential to correctly plan a proper treatment strategy. Even to an experienced subspecialty pathologist in referral centers, this could be challenging because of non - specific presentation, overlapping appearance of different neoplasms, and the large miscellany of different possible histologies. [3] Multimodality therapy regimens, including surgery, radiotherapy (RT), and/or chemotherapy, are frequently utilized in the treatment of these tumors. Although surgery followed by adjuvant radiation is most commonly used, there is no consensus for the role of chemotherapy/systemic therapy or definitive sequence of treatment modalities. [4] Therefore, here we presented a case report of SCC sinonasal.

2. Case Report

A 43rd years old male, came to the ENT outpatient department with a chief complain of a mass on the nose since one and a half years before. The mass was progressively getting bigger from five months before. There was an edema on the eyes and palate. He had already done a CT scan on August 2022 at Kerta Usada Hospital. There was no previous history, medical history, family history and allergic history. He was referred from Kertha Usada Hospital to Bali Mandara Hospital at March 18th 2024 with ad diagnosis of tumor sinonasal suspected carcinoma.

The patient looked good and alert (E4M6V5). Blood pressure was 122/78 mmHg, heart rate 112 x/minute, respiratory rate 20 x/minute, temperature 36.5ºC and oxygen saturation 99%. From the physical examination, it was found a mass on the nose.

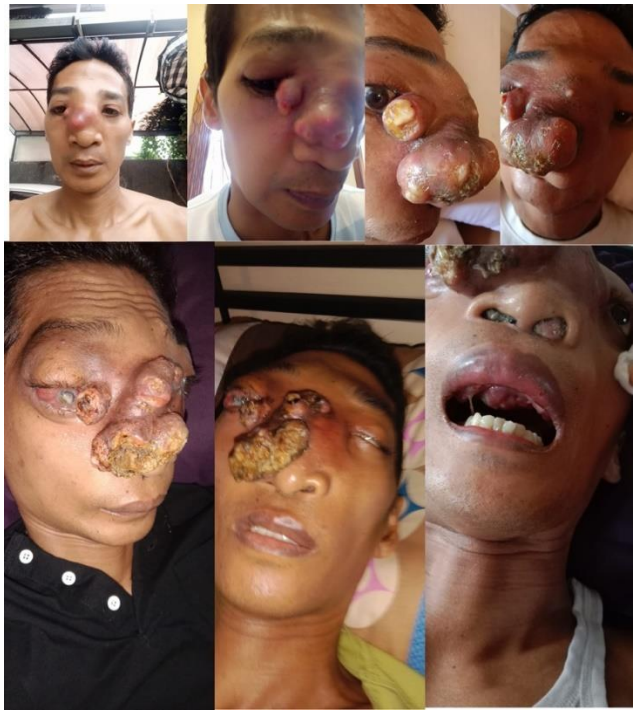

Figure 1

Figure 2: Clinical picture of the patient before chemotherapy

His laboratory results at March 25th 2024, showed anemia (Hemoglobin levels 10.6 g/dL, hematocrit 32.4%), leucocyte 9.57 x 10^3/uL, platelet 543 x 10^3/uL, neutrophil 78.3%, monocyte 8.9%, lymphocyte 12%, and NLR 6.5. Bleeding time and clotting time were normal. At April 8th 2024, SOGT (AST) was 22 U/L, SGPT (ALT) was 13 U/L, urea was 51 mg/dL, creatinine serum 0.84 mg/dL, natrium 127 mmol/L, and kalium 4.6 mmol/L.

He was diagnosed with bilateral sinonasal tumor. He was scheduled for tumor biopsy and found a SCC sinonasal stage IVA. He was given paracetamol 500 mg every 8 hours, tranexamic acid 500 mg every 8 hours, and cefixime 100 mg every 12 hours. He was scheduled for chemotherapy at April 8th 2024 with Paclitaxel 270 mg and Carboplatin 690 mg. He was scheduled for second chemotherapy at April 30th 2024.

Figure 3: Clinical picture after the first chemotherapy

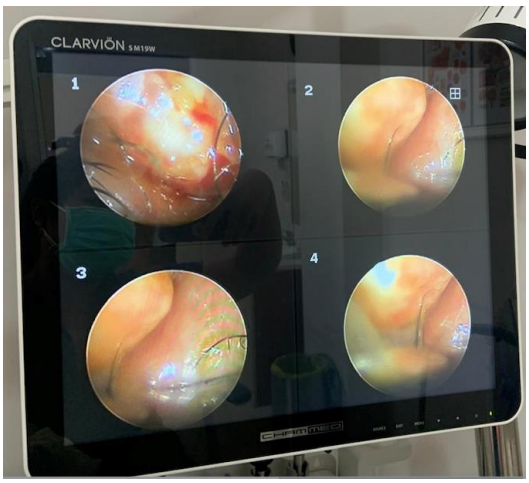

Figure 4: Nasal endoscopy image after the first chemotherapy.

3. Discussion

Squamous cell carcinoma (SCC) of the sinonasal tract (SNSCC) is "a malignant epithelial neoplasm arising from the surface epithelium lining the nasal cavity and paranasal sinuses and exhibiting squamous differentiation". Despite this relatively simple definition, SNSCC includes a wide group of tumors with heterogeneous biological features, as witnessed by the fact that its genetics showed partial overlap with respect to other sinonasal cancers, such as sinonasal undifferentiated carcinoma (SNUC) and neuroendocrine carcinomas (NEC). [3]

The incidence of SNSCC in males is 0.52 cases per 100, 000 patients, and females 0.23 cases per 100, 000 patients, with a male to female incidence ratio of 1.85–2.26: 1. [2] Almost 80% of patients were 55 years old or older. [3] Smoking status is associated with worse outcomes in SNSCC, with current

smokers having a decreased 5 - year OS compared with reformed smokers. Worse outcomes are also seen in patients with poor performance status and African American patients, similar to the HNSCC overall. [2] Our case, was a 43rd years old male. There was no history of smoking.

SNSCC is a complex disease, and its pathogenesis is poorly understood. Occupational exposure to several industry compounds, such as wood dust, leather dust, glue, chrome, nickel, formaldehyde, arsenic, welding fumes, and multiple compounds in the textile industry, has been reported to increase the risk of SNSCC. Squamous cell cancers in several anatomic locations, including the oropharyngeal region, are well known to be linked to human papillomavirus (HPV) and recent studies support a potential causative role for the virus in SNSCC as well. Its relationship to sinonasal SCC is less direct. Recent studies have found transcriptionally active HPV in 40.9% of sinonasal SCC, with a higher incidence in variants such as basaloid (46.2%), papillary (80%), and adenosquamous (66.6%). [5, 6] The contribution of genetic abnormalities to the pathogenesis of SNSCC is poorly understood. TP53 mutations in the tumor have been described in 80% of SNSCC, followed by KRAS mutations, EGFR mutations, FGFR1 amplification, SOX2 amplification, and VEGFR gene overexpression. [6] Our patient was sinonasal SCC. History of HPV infection was not identified.

The histology of the sinonasal tract is diverse. The nasal vestibule is composed of keratinized squamous epithelium, and has sweat glands, hair follicles, and sebaceous glands. Approximately one to two centimeters into the nose at the limen nasi this epithelium transitions to a ciliated pseudostratified columnar epithelium, also called the Schneiderian epithelium, which lines most of the nasal cavity and paranasal sinuses, contains submucosal seromucous glands. The mucus membrane of the paranasal sinuses is thinner than that of the nasal cavity and has fewer seromucous glands. The olfactory mucosa is located over the cribriform plate and the superior third of the nasal septum. It consists of specialized olfactory neuronal cells that protrude from the mucosa alongside columnar sustentacular epithelial cells. [6]

Histologic diagnosis of SNSCCs can be challenging due to relative rarity, a large miscellany of different possible histology, and overlapping appearance of other malignancy or inflammatory disease. Both keratinizing and nonkeratinizing types of squamous cell carcinoma are encountered. [3, 6] Various histological subtypes of SCC exist with four degrees of differentiation (G1: well - differentiated, G2: moderately differentiated, G3: poorly differentiated, and G4: undifferentiated). In head and neck SCC, histological differentiation often predicts biological behavior, including local invasion and possibly regional or distant spread, and generally, poorly differentiated tumors are more aggressive than well - differentiated ones. This is particularly true in nasopharyngeal carcinoma as nonkeratinizing carcinoma has been shown to have improved survival compared with keratinizing SCC. [4]

Early symptoms are non - specific and include nasal obstruction, along with epistaxis, facial pain, or persistent rhinorrhea. Locally advanced disease has more localizing symptoms such as proptosis, diplopia or cranial neuropathy, chronic rhinosinusitis, or headache. Symptoms of advanced disease correlate to location and extent of disease. Tumors advancing towards the anterior cranial fossa via the cribriform plate or the orbit cause anosmia or proptosis, whereas tumors extending to the lateral bony wall into the cavernous sinuses cause neuropathy of cranial nerves III, IV, VI, V1, and V2, leading to diplopia and paresthesia of the face. When the tumor invades the middle cranial fossa, patients experience paresthesia of the lower face or trismus due to involvement of cranial nerve V3 or invasion of the pterygoid muscles. Because many of the early symptoms are associated with common benign states such as allergies, most patients with these tumors tends to be diagnosed when it is locally advanced, or even metastatic. Primary tumor locations are maxillary sinus (60%) and/or nasal cavity (25%), commonly. Diagnosis of SNSCC most often occurs at an advanced stage due to nonspecific symptoms early in the disease, with >80% of patients reportedly presenting with at least stage T3 disease. [5, 6] Our patient symptoms was a mass on the nose since one and a half years before. The mass was progressively getting bigger from five months before. There was an edema on the eyes and palate.

SNSCC are characterized by aggressive bony destruction of the adjacent sinus walls. Invasion of the contralateral sinonasal area, orbital wall, infratemporal fossa, and skull base is sometimes observed, which needed a combination of CT and MRI for the most accurate assessment of tumor extent. Due to its high spatial resolution, CT is required to visualize the structural changes and reabsorption of thin bone structures. Gadolinium - enhanced MRI is valuable to assess soft tissue involvement, which can otherwise resemble other conditions such as lymphoma, necrosis, inflammatory, mucus retention, and fibrosis. Apparent diffusion coefficient (ADC) values are also useful in differentiating sinonasal lymphoma as the ADC values of maxillary SNSCC are typically higher than those for lymphoma. PET - CT can be used as “metabolic biopsy” to characterize sinonasal malignancy. PET - CT of SNSCC arising from ISP found an overlap in fluorodeoxyglucose (FDG) uptake values among some histologic subgroups. PET - CT has also been used as a prognostic tool. A retrospective study described that absence of pathologic FDG uptake at the first post - treatment PET - CT was associated with better OS. [6] He was done a CT scan on August 2022 at Kerta Usada Hospital.

Preoperative diagnosis has been reported to be non - concordant to the final histopathological diagnosis in 7–10% of HN cancers. Not surprisingly, the highest rate of discrepancy was found in the sinonasal tract, with misdiagnosis observed in 23.8%. Of note, while SCC is the most common histology among cancers arising from the maxillary sinus, a pretreatment diagnosis of SCC has been associated with the lowest diagnostic reliability rate (50%) in tumors centered in the nasoethmoidal area. [3]

Multimodality therapy regimens, including surgery, radiotherapy (RT), and/or chemotherapy, are frequently utilized in the treatment of these tumors. Although surgery followed by adjuvant radiation is most commonly used, there is no consensus for the role of chemotherapy/systemic therapy or definitive sequence of treatment modalities. [4] Surgery is a potentially curative treatment for resectable SNSCC with the

goal of complete resection and achieving negative margins. Due to the proximity of the nasal cavity and paranasal sinuses to critical structures, complete resection can be prohibitively morbid. The surgical approach, including endoscopic or open surgery, should be selected based on tumor location and local extension. [6] For patients undergoing surgery, endoscopic endonasal surgical resection is increasingly utilized and favored, when feasible, over traditional open surgical resection due to decreased morbidity with similar outcomes. Five - year overall survival (OS) of sinonasal SCC is ~50%, without significant improvement in survival over the past decades. [4, 7]

To achieve negative surgical margins, the use of induction chemotherapy has been investigated as part of multimodal treatment. In the past decade, multiple studies have shown promising results of induction chemotherapy by improving morbidity, function/organ preservation, and overall survival. [6] Induction chemotherapy (IC) can be utilized as a strategy to promote organ preservation. [8, 9] He was scheduled for chemotherapy at April 8th 2024 with Paclitaxel 270 mg and Carboplatin 690 mg.

Adjuvant intensity - modulated RT (IMRT) after complete resection is considered the standard treatment for pT2 - T4 SNSCCs, aiming to decrease the incidence of local recurrence. Compared to conventional 2D and 3D techniques, IMRT for the management of unresectable T4 paranasal sinus and skull base malignancy may help preserve organ function and minimize toxicity. Intensity - modulated particle therapy (IMPT) such as protons and 12C - carbon ions are also being investigated for these patients and allows the design of a sharp dose gradient to a well - defined depth, leading to much higher radiobiological effectiveness and reduced dependence on tissue oxygenation. Concurrent platinum - based adjuvant therapy is often delivered to further optimize tumor control. The aim is two - fold, both radiosensitization and targeting of residual disease in cases of positive margins, with high - risk features, such as nodal, perineural or lymphovascular invasion. The dose and schedule of cisplatin typically used is either 100mg/m^2 every 3 weeks or 30–50 mg/m^2 weekly. Carboplatin can be considered if the patient is ineligible for cisplatin. [6, 10]

Definitive chemoradiation therapy is employed for patients with unresectable tumors or for those who do not choose to undergo surgery. The chemotherapy is platinum - based as above delivered using the same schedule described above in the adjuvant setting. Radiation is typically delivered in the form of IMRT, concurrent with chemotherapy. Currently, there are no prospective data comparing these two forms of radiation. A phase II study investigating the efficacy and toxicity of intensity - modulated or proton radiation therapy for locally advanced sinonasal malignancy is ongoing. For locoregional recurrence, salvage surgery or re - radiation is generally recommended, if possible. Palliative regimens were either platinum - , anthracycline - , taxane - , and/or alkylating - agent - based (e. g., temozolomide or ifosfamide) in different combinations. [6]

Ackall et al., stated that chemotherapy within the treatment regimen did not confer survival benefit except in surgical patients when positive margins were present, and surgery with adjuvant chemoradiation trended toward improved survival. [4] Teitelbaum et al., found that patients who underwent surgery with adjuvant RT had better overall survival (hazard ratio [HR], 0.74; P <.001; 95% CI, 0.63 - 0.86). As for treatment volume per facility, 7.4% of patients were treated at a low - volume center, 17.5% at a medium - volume center, and 75.1% at a high - volume center. Univariate analysis showed that treatment at a high - volume facility conferred a significantly better overall survival (HR, 0.77; P =.002). Multivariable Cox proportional hazards regression analysis, adjusting for age, sex, tumor classification, and treatment regimen, demonstrated that patients who underwent treatment at a high - volume facility (HR, 0.81; P <.001) had significantly improved survival. [11] Mur et al., stated that induction therapy was safe and effective. When compared with SOC, induction therapy improved 3 - year overall survival. [9]

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